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sorghum, algae such as *Chlamydomonas reinhardtii* and *Chlorella*, mammals such as mouse, rat and human fish such as trout, bluegill, carp, cyprinodont, guppy, zebra fish and fathead minnow, insects such as fly, mosquito, cockroach, greasy grind, dragonfly and silkworm moth.

34. The method of claim 28, 29, 30, or 31, wherein said DNA fragment coding for enzyme protoporphyrinogen comprises SEQ ID NO:2 or SEQ ID NO:10.--

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REMARKS

The Office Action of November 24, 1999 presents the examination of claims 1-7. Claims 1-7 are herein cancelled. New claims 28-34 are added for the Examiner's consideration. Support for the new claims is found in the instant specification. No new matter is inserted into the application.

Election/Restriction

In response to the Restriction requirement issued in the pending application, Applicants elect Group I, claims 1-7 with traverse. Reconsideration of the claims and withdrawal of the instant Restriction is respectfully requested.

Applicants respectfully submit that the Examiner has not established that there is an undue burden in searching for all claims as required by MPEP § 803. Applicants note that only two

classes, 435 and 536, must be searched in order to properly examine the instant application. However, the Examiner does not state or imply that searching two classes will create an undue burden for the Examiner. Therefore, the Applicants can only assume that an undue burden for searching does not exist. Further, Groups II and III are even members of the same subclass. Thus, it would not be an undue burden to search the claims of Groups II and III together.

For the above reason, Applicants respectfully request that the restriction requirement be withdrawn, and Groups I through III, or at least Groups II and III, be recombined.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejects claims 1-7 under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter not described in the specification. Claims 1-7 are canceled, thereby rendering the instant rejection moot. Nonetheless, Applicants wish to provide remarks clarifying the instant invention, as recited in the new claims 28-34.

The Examiner rejects claims 1-5, allegedly drawn to a protoporphyrinogen oxidase gene, because the complete structure of the gene is not described in the specification. Applicants wish to clarify that instant claims 28-34 are drawn to a method of using the PPO gene, rather than claiming the gene itself.

Thus, Applicants submit that it is not necessary to disclose the complete structure of the gene.

In any event, the structures of the PPO genes are well known in the art. For example, other PPO genes have been described in journal articles. Further, the method of claim 1, and new claim 28, will work with PPO genes other than the rat and *Chlamydomonas* PPO genes disclosed in the instant specification. The instant specification describes how to obtain these PPO genes from other species specifically on page 30, lines 17-20. Thus, acquiring and using other PPO genes in the present method would not constitute undue experimentation for one of ordinary skill in the art.

The Examiner rejects claim 5 for allegedly claiming the PPO gene from all animals and plants when only the rat and yeast PPO sequences are disclosed. Again, Applicants wish to emphasize that the instant claims are method claims, wherein a method for evaluating the ability of a compound to inhibit PPO activity, for example, is claimed. The "PPO gene" is not claimed *per se*. Thus, the rationale for the instant rejection is improper. Nonetheless, Applicants submit new claim 33, wherein the species (as recited on page 8, lines 14-19 of the instant specification) from which the PPO gene may be derived are listed.

Claim 7 is also rejected by the Examiner for claiming a microorganism when only yeast and *E. coli* are disclosed as host cells in the specification. In response to the Examiner's

remarks, Applicants submit new claim 32, wherein "microorganism" is an *E. coli* or a yeast cell. Thus, the instant rejection is overcome.

The Examiner also rejects claims 1-7 under 35 U.S.C. § 112, first paragraph, for allegedly not being described in the instant specification. Claims 1-7 are cancelled, thus rendering the instant rejection moot. Nonetheless, Applicants wish to provide remarks clarifying the instant invention, as recited in the new claims 28-34.

Specifically the Examiner argues that the specification does not give adequate guidance to determine whether the host compound is an inhibitor of PPO, or if said compound is affecting the growth of the host cell through other means. Applicants respectfully disagree. In fact, the method of the present invention easily determines whether or not growth inhibition of a transformant is due to addition of a growth compound that directly inhibits PPO.

In the present method, a comparative system is utilized wherein a transformant is cultured in a medium containing substantially no protoheme compounds. In a first test, for example, a test compound is added to the system. In a second test, for example, the same test compound is not added to the system. The growth of the transformant in the two systems is compared. If the growth of the transformant in the presence of the test compound is inhibited compared with the growth of the

transformant in the absence of the test compound, then the test compound is somehow affecting growth negatively. At this point, then, whether or not the test compound is affecting the PPO pathway must be determined.

In order to confirm that the test compound is indeed inhibiting the growth of the transformant, the transformant is then cultured in a medium containing protoheme compounds. Said protoheme compounds are required for maintaining the growth of the transformant. Under normal circumstances, when PPO is inhibited, most if not all heme synthesis is terminated. When protoheme is present in the medium all transformants will grow, regardless of whether PPO inhibition is present. Therefore, it is irrelevant whether PPO inhibition is present, because the transformant is directly obtaining protoheme from the medium.

In a next step, the test compound, which is believed to cause growth inhibition, is added to the medium. At this point, the growth of the transformant may be affected. If the growth of the transformant is affected negatively, i.e. the growth is suppressed, then the test compound affects growth by a mechanism other than the PPO pathway. Again, the transformant is receiving protoheme from the medium, thus the PPO pathway is bypassed. Thus, it can be concluded that the test compound does not affect the PPO pathway.

Conversely, if the growth is not affected, then no conclusions as to whether the PPO pathway is functioning or not

can be made. This situation is identical to the first step above.

Applicants submit that the instant claims 28-34 meet the requirements of 35 U.S.C. § 112, first paragraph, and thus should be placed into a condition for allowance.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 1-7 under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. Claims 1-7 are canceled, thereby rendering the instant rejection moot. Applicants herein submit new claims that more clearly describe the present invention. Applicants respectfully submit that these claims meet the requirements of 35 U.S.C. § 112, second paragraph, and thus should be found allowable.

Overall, Applicants submit that the instant claims are fully in compliance with 35 U.S.C. § 112, first and second paragraphs. Further, all of the present claims define patentable subject matter such that this application should be placed into condition for allowance. Early and favorable action on the merits of the present application is thereby requested.

If there are any minor matters precluding allowance of the present application which may be resolved by a telephone discussion, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at (703) 205-8000.

Serial No.: 09/289,180

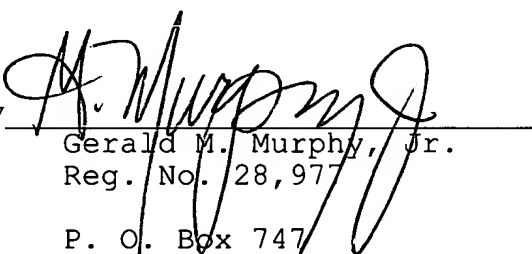
Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of three (3) months to May 24, 2000 in which to file a reply to the Office Action. The required fee of \$870.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By


Gerald M. Murphy, Jr.
Reg. No. 28,977

P. O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000


GMM/KLR/gh